PROGNOSTIC SIGNIFICANCE OF HIGHLY SENSITIVE C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE PATIENTS

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"PROGNOSTIC SIGNIFICANCE OF HIGHLY SENSITVE C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE PATIENTS"** submitted by **Dr.J.RAJ KUMAR** to the Tamil Nadu Dr. M.G.R.Medical University, Chennai in partial fulfillment of the requirement for the award of M.D Degree Branch I (General Medicine) is a bonafide research work was carried out by him under my direct supervision & guidance.

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DECLARATION

I, **Dr.J.RAJ KUMAR** declare that, I carried out this work on, "**PROGNOSTIC SIGNIFICANCE OF HIGHLY SENSITIVE C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE PATIENTS**" at the Department of Medicine, Govt. Rajaji Hospital during the period of March 2012 to October 2012. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any other University, Board either in India or abroad.

This is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.

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CONTENTS

INTRODUCTION

Stroke is now considered as an important health problem for all individuals and society. After Acute myocardial infarction and malignancy, Ischemic stroke is the third leading cause of death and is also as leading cause of hospitalization causing disability. So we have to identify the stroke at an earlier date which help the treating physicians to plan treatment, make interventions and to provide significant benefit to the people and community and to save the patient . The conventional risk factors namely blood pressure (BP), smoking, diabetes, dyslipidemia, alcohol predict the happening of stroke, but still they are not completely reliable, therefore there is a continuous debate and search for prediction of occurrence of stroke and reliability of prognostic markers in stroke have gained interest in recent years.

When an individual is exposed to any insult in terms of infection and injury, there is a production of proteins called Acute Phase Proteins. This Acute phase protein participates in all inflammatory process and plays a major role in both acute and chronic inflammatory states. The Acute phase reactants are fibrinogen, ferritin, haptoglobin, highly sensitive C – reactive protein, Complements (C3), Complements (C4), Tumour necrosis factor. Among these

various proteins, Highly sensitive C-reactive protein have gained wide recognition in monitoring different diseased states and it leads to the development of reliable and fast assay measuring their plasma levels.

In recent years, inflammatory process plays an important role in pathophysiology of stroke. The initiator of extrinsic pathway of coagulation is Tissue factor. This tissue factor got expressed when mainly monocytes are stimulated by C-reactive protein and initiates vascular thrombosis. hsCRP, a marker of Atherosclerosis and also a peripheral marker of inflammation found to be valuable in sorting out of possible risk factors of subsequent cerebrovascular and cardiovascular (CV) events, Peripheral Arterial Diseases or death. This important fact was also supported by abundant laboratory and experimental evidence demonstrating that atherosclerosis refers to chronic inflammatory process.

High plasma levels of CRP are not specific to disease, but it is sensitive marker and is produced in response to tissue injury, infectious agents and inflammation. hsCRP predicts the first cardiovascular event in general populations . hsCRP is the only inflammatory marker which independently predicts the future risk of stroke when measured prior to onset of clinical disease.

hsCRP is now widely determined as valuable and good prognostic indicator in stroke because of the following reasons:

- Severity of stroke correlates positively with hsCRP concentration and these levels also denotes the degree of inflammation secondary to infarction of the brain.
- Reflects the underlying Atherosclerotic Disease.

AIMS & OBJECTIVES

1) To evaluate the prognostic significance of hsCRP with severity of stroke in correlation with stroke scales (NIHSS and MRS).
2) To evaluate the relationship between hsCRP and various risk factors for stroke, with territory of infarct and other findings in CT film.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Stroke was first recognized by Hippocrates, the Father of Medicine about 400 BC. During that period, Stroke was described as Apoplexy which denotes “Struck down by Violence” in Greek .[1]

In 1658, Johann Jacob Wepfer states that stroke occurs predominantly due to disruption of blood flow to the brain. In 1847, Rudolf Karl Virchow, who is a German pathologist, identified atherosclerosis and clotting mechanism is the definitive cause of ischemic stroke. [2]

Hounsefield introduced the concept of Computed Tomography in mid-1960s, which helps in the clear distinction between brain ischemia and haemorrhage. Then Magnetic Resonance imaging was introduced in mid 1980s which remains superior to CT scans and it helps to identify posterior fossa lesions.[1] In 1950, Craven identified aspirin as an anticoagulant property and it was used for stroke only by mid 1970s . Thrombolytic therapy for ischemic stroke was introduced in early 1960s, but only in 1995 it was approved by United States Food and Drug Administration for thrombolytic therapy for ischemic strokes.[1]

Stroke or cerebrovascular accident is defined by abrupt onset of a Neurologic deficit that is due to focal vascular cause.

EPIDEMIOLOGY

In United states, stroke now ranks as third common cause of death, after myocardial infarction and cancer**,** it also considered as leading cause of disability.[6] Among 7,00,000 cases of reported strokes (includes 6,00,000 cases of Ischemic stroke and 1,00,000 cases of haemorrrhages, intra cerebral, sub-arachnoid haemorrhages), about 20% of cases were dying within one year of incidence of stroke. If such incidence continues, this number will reach 1 million cases per year by 2050.[7] Stroke accounts for 5.7 million deaths and 16 million first ever cases worldwide in the year 2005 .[8]

In India, about 1 million cases were reported in the year 2003, for every one lakhs population in the people of age group more than 20 years and it also contributes 1.2 % of the total deaths.[9] In the study conducted by Banerjee and Das, reports age adjusted prevalence rate ranges between 250 -350 per one lakhs Population.[12] As per Indian Council Medical Research (ICMR) reports, that Stroke accounts for 41% mortality and 72% morbidity (Disability Adjusted Life Years) among the non communicable diseases.[10] Stroke and

diabetes together brings the estimated national economic loss of approximately 9 billion dollars in India between 2006 to 2015. Based on the incidence of stroke study reported from Eastern India, the adjusted annual incidence was 124 in rural areas, [13] and 145 in urban areas .[14]

CLASSIFICATION OF STROKE [5]

Stroke can be classified in different ways.

Based on Clinical features: [22]

1. Completed stroke
2. Stroke in Evolution
3. Transient Ischemic Effects
4. Reversible Ischemic Neurological Deficit

Based on Anatomical Location:

1. **By vascular supply**
    a. Carotid artery
    b. Vertebrobasilar artery
2. **By location**
    a. Supra-tentorial which includes lobar and Capsulo-gangilionic
    b. Infra-tentorial which includes brainstem and cerebellum

3. **Based on Etiology**

By pathology

a. Ischemic

b. Haemorrhagic

ETIOLOGY [3]

Common causes	**Uncommon causes**
Thrombosis Large vessel thrombosis Lacunar stroke (small vessel) Dehydration Embolic Occlusion Cardio –embolic Myocardial infarction Mural thrombus Atrial fibrillation Dilated cardiomyopathy	Cardiogenic Marantic Endocarditis Libman sacks Endocarditis Intracardiac mass Mitral valve calcification Atrial myxoma Vasculitis Primary CNS vasculitis Systemic Vasculitis – Wegener's Granulomatosis, Polyarteritis Nodasa, Takayasu arteritis , Giant Cell arteritis ,

Valvular lesions –mechanical valves, Mitral stenosis, bacterial endocarditis Atrial sepal aneurysm Spontaneous ECHO contrast Paradoxical embolus- Patent Foramen ovale , Atrial septal defect Artery to Artery Aortic arch Carotid artery bifurcation Arterial dissection	Meningitis (Tuberculosis, syphilis, bacterial, fungal, Bacterial, Zoster) Hypercoagulable disorders Antiphospholipid Antibody Syndrome, Protein C deficiency, Protein S deficiency, Antithrombi III deficiency , Prothrombin G20210 mutation , Systemic lupus erythematosis, Thrombotic thrombocytopenic Purpura , Disseminated Intravascular coagulation, systemic Malignancy , thalessemia , Inflamamtory bowel disease, Oral

	Contraceptive pills, Homocysteinmia. Dysproteinemias Eclampsia,Moyamoya disease Drugs –cocaine, Amphetamine . Subarachnoid haemorrhage vasospasm

RISK FACTORS[15]

IRREVERSIBLE	MODIFIABLE
Age Sex (male > female, not applicable in very young and very old) Hereditary Race (Afro-carribean population >Asian population> European population)	Raised Blood Sugar Hypercholesterolemia Elevated Blood pressure Smoking Sickle cell Anaemia Polycythemia Excessive consumption of alcohol Cardiac Causes 1. Atrial fibrillation 2. Infective endocarditis 3. Heart ailure 4. Hypertrophy of left ventricle 5. Recent myocardial infarction 6. Congenital heart disease and malformations

	7. Mitral stenosis Oral contraceptive pills Physical inactivity Head and neck injuries

AGE:

People of any age group can be affected by stroke. Incidence of stroke increases with increasing age.

SEX:

Men are more commonly affected with stroke than women. Young stroke is more common in young female using oral contraceptive pills and in pregnant individuals.

RACE:

The occurrence of ischemic stroke is more common among the Asians and Blacks.

HYPERTENSION:

The risk of stroke is increased four to six times in hypertensive patients. Since hypertension promotes the atheroma formation in all sized vessels of brain, hypertension is considered as important risk factor for stroke.

DIABETES:

Diabetic individuals are three times more prone for than individuals who are not diabetic. Diabetes also promotes the atheroma formation, thereby increasing the rate of occlusion of intracranial arteries.

SMOKING:

Smoking increases the stroke risk by two times. Smoking causes vasoconstriction, increases fibrinogen concentration, causes polycythemia, reduces aggregation of platelets, all these contributes stroke occurrence.

ALCOHOL:

High Alcohol Consumption increases the risk of stroke .

Syndromes of cerebral infarction.[16]

Carotid Artery occlusion

1. Amaroux fugax which is also known as transient monocular blindness.
2. Speech disorder
3. UMN type of facial palsy
4. Loss of sensation in one half of the body(cortical type of sensory loss)
5. Weakness of one half of the body

6. Hemianopia

Anterior cerebral artery Infarct[23]

When anterior cerebral artery is blocked distal to the anterior communicating Artery, patient will have following features

- ❖ Contalateral hemiplegia and hemisensory loss with predominant lower limb involvement
- ❖ No facial involvement
- ❖ Urinary incontinence
- ❖ Emotional disturbances
- ❖ Presence of released reflexes

When anterior cerebral artery is blocked proximal to the anterior communicating Artery, patient will have

- ❖ Complete hemiplegia which denotes hemiplegia and facial involvement on the opposite side of the body with or without aphasia.

Middle cerebral artery infarcts

Occlusion of Stem of Middle cerebral artery causes

a. global aphasia
b. contralateral hemiplegia
c. contralateral hemianaesthesia

d. contralateral hemianopia
e. apractagnosia, dysarthria, contralateral neglect in non dominant hemisphere involvement.

Occlusion of proximal superior division of MCA will cause motor weakness, sensory disturbances and motor aphasia.

Occlusion of Inferior division of MCA will cause

- Wernicke's aphasia without weakness
- Sometimes quadrantopsia
- In non dominant hemisphere, hemineglect and spatial agnosia can occur without weakness.

Posterior cerebral artery syndrome[22]

Signs and symptoms	**Structures involved**
Homonymous hemianopia	Calcarine cortex
Cortical blindness, denial of blindness, apraxia of ocular movements	Bilateral occipital lobe involvement
Dyslexia without agraphia	Dominant calcarine lesions
Memory defect	Dominant temporal lobe

prosopagnosia	Non dominant calcarine and lingular gyri
Simultagnosia	Bilateral visual cortex

Vertebral artery Occlusion

Wallenberg's syndrome occurs due to the Posterior inferior cerebellar artery occlusion (PICA), vertebral, or superior, middle or inferior lateral medullary arteries. This syndrome is characterized by contralateral impaired pain and temperature sensation (spinothalamic tract involvement) and the same side Numbness over half of the face, ataxia, Horner's syndrome, dysphagia, vertigo, hiccups and loss of taste sensation.

Basilar artery syndrome

Complete basilar artery syndrome causing coma due to ischemia of high midbrain reticular activating system, quadriparesis along with facial involvement, ophthalmoplegia and loss of corneal and pupillary reflexes. In contrast, partial basilar artery syndromes will usually results in locked-in syndrome, top-of-the-basilar syndrome.

In locked in syndrome, the pathology is infarction of base of Pons resulting in quadriparesis along with loss of facial expressions, loss of

horizontal eye movements. Consciousness is retained due to sparing of reticular activating system, but vertical movement of eye is present.

In top-of-the-basilar syndrome, the presenting clinical picture will be hemianopia or complete cortical blindness, amnesia vertical gaze palsies, and hallucinations.

Single perforating artery Occlusion

'Lacunar syndrome' occurs mainly due to the occlusion of one of many arterioles which arises perpendicularly from large parent artery to supply little areas in deep areas of brain and brain stem. Here, the affected individual will not have any features suggestive of aphasia, hemianopia, neglect and conjugate deviation of eyes.[4]

Clinical features[3]	**Structure involved**
Pure motor hemiparaesis	Infarct in the posterior limb of Internal capsule, basis pontis
Pure sensory stroke	Ventral thalamus infarct
Ataxic Hemiparaesis	Ventral pons infarct
Dysarthria and clumpsy hand syndrome	Genu of internal capsule infarct

PATHOPHYSIOLOGY OF ISCHEMIC STROKE[3]

Ischemia occurs due to the acute occlusion of intra-cranial vessels resulting in reduction in blood flow to brain tissues. These amount of blood flow reduction depends on location of blood vessels, site of occlusion, adequacy of collateral blood vessels and blood pressure.[3]

Amount of blood flow\ gram brain tissues\ minute	**Effect on brain tissues due to decreased blood flow**
Zero	Death
< 16 -18 ml	Infarction (within 1 hour)
< 20 ml	Ischemia(without infarction, if it is not prolonged for several hours or weeks)

ISCHEMIC PENUMBRA

ISCHEMIC PENUMBRA is a dense central core surrounded by a less dense zone of Ischemia but function can be reversed and restoring the blood perfusion prevents the death of brain tissues. The viability of neuronal cells in

these is 3 hours, so blood flow should be restored by adopting various reperfusion techniques and or neuroprotective agents, hence this period is considered as “Therapeutic Window period”.[5] This zone can be detected in the CT or MRI using Diffusion perfusion imaging.[3]

PATHOGENESIS

Cerebral infarction occurs due to two different mechanisms namely necrotic and apoptotic mechanisms. In this necrotic mechanism, starvation of neurons causes mitochondrial dysfunction which causes energy failure which in turn leads on to neuronal depolarization. These causes increase in intracellular calcium ions and increased glutamate release from synaptic terminals, which leads on to neurotoxicity.[3] Energy failure also causes lipolysis and release of free radicals , platelet activating factors, arachidonic acid and all these results in neuronal injury.[5] In ischemic penumbra, apoptotic pathway operates causes neuronal cellular death in days or weeks later . Fever and hyperglycemia (>200 mg/dL) causes detrimental effects in outcome of stroke and they further worsens ischemia and promotes cellular death.[3]

Among the ischemic stroke incidence, cardio-embolism constitutes 20%. In heart disease, thrombi attached to left heart wall, atrial, ventricular wall detach and enters systemic circulation, these thrombi lyses quickly and causes

Transient Ischemic Attacks or stroke. These Emboli lodges frequently in Middle cerebral Artery or Posterior cerebral Artery but rarely in anterior cerebral artery.[3]

ATHEROSCLEROSIS

Atherosclerosis is one of the major causes of death and atherosclerosis of coronary arteries, intracranial and extra cranial vessels, peripheral arteries causes coronary artery disease, cerebrovascular accidents, intermittent claudication respectively.[3] The characteristic feature of Atherosclerosis is Atheromas which is formed by thickening of tunica intima and accumulation of lipids. The atheromatous plaques consists of central core which is formed by cholesterol esters and cholesterol and it is covered by a fibrofatty plaques and this forms a raised lesion in the tunica intimal layer.These atheromatous plaques will undergo changes such as calcification, ulceration or rupture of thrombus and exposes the underlying thrombogenic materials resulting in superadded thrombus formation.[17]

RISK FACTORS FOR ATHEROSCLEROSIS[17]

Non modifiable risk factors are Elderly age, male sex, genetic predisposition, whereas potentially modifiable risk factors are diabetes mellitus, hypertension, cigarette smoking, and hypercholesterolemia. And the

less quantifiable risk factors are sedentary life style, central obesity, increased stress, hyperhomocysteinemia, increased alcohol consumption, estrogen deficiency in post menopausal women;etc.[17] About 20% of ischemic stroke occurs due to carotid atherosclerosis and in carotid arteries; common carotid atery bifurcation and proximal internal carotid artery are the most common sites for atherosclerosis.[3]

IMAGING STUDIES

CT SCANS

CT scan helps in the clear differentiation between haemorrhages and infarct and it also helps to detect abscess, tumour mass lesions, extra parenchymal haemorrhages (extra dural and sub dural haemorrhages).[3]

Merits:

1. CT distinguishes infarct and haemorrhages and helps the treating Physician to decide the line of management. .
2. CT scans are highly sensitive in detecting Subarachnoid Haemorhage.

Demerits:

1. When CT scans are taken in an acute set up, ct scans will not usually detect the infarct in the first 24 to 48 hours.
2. CT scans misses the small infarct on the cortical surface.

3. Usually CT scans will not detect the posterior fossa lesions due to artifact (bone).

INFARCT: CT scans shows infarct as a hypodense lesion**.** When there is hypodense marking of particular vein, gray enhancement and post contrast enhancement of that particular vein in CT scans, such finding favors thrombosis of cortical veins of the brain.

HAEMORRHAGE: Hyperdense lesions or areas in the film indicates haemorrhages. About 1cm or more in diameter haemorrhages will be detected in CT scans.

CT FINDING IN CEREBRAL INFARCTION[18]

Timing of Infarct	**CT Findings**
Hyperacute (<12 hours)	Lentiform Nucleus obscuration Increased dense lesions (25 – 50 %) Normal (50%)
Acute (12 to 24 hours)	Effacement of sulcus, Insular ribbon sign– loss of grey and white matter differentiation.
Days 1 day to 7 days	Transformation of infarct into haemorrhages, Enhancement of Gyrus, Mass effect, Low

	density areas which is wedge shaped, involving white and grey matter.
Weeks :1-8	Resolving of mass effects, persistence of contrast enhancement.
Months to year	Encephalomalacia changes. Loss of Volume

MRI SCANS[3]

1. Posterior fossa infarction and cortical infarction can be easily identified in these scans and so it was considered superior and more sensitive than CT scans in such lesions.
2. Early brain infarction can be easily determined by Diffusion weighted images and this imaging modality is more sensitive.
3. Stenosis of intracranial vessels and extracranial internal carotid arteries stenosis were detected by MR Angiogram.

COMPLICATIONS OF STROKE[15]

1. Aspiration Pneumonia, Urinary tract infection
2. Bed sores.
3. Pulmonary embolism with Deep vein thrombosis.

4. Contractures.

5. Dehydration.

6. Hypoxemia

7. Hyperglcemia

8. Frozen Shoulder and subluxation

9. Constipation

10. Dehydration, Hyponatremia and seizures.[15]

TREATMENT

The laboratory investigation and treatment of stoke should be done in proper order as soon as clinical diagnosis of stoke is made.

Goal of treatment: prevention of brain injury or reversal of ischemic brain damage.

General treatment strategies of Stroke treatment

1. Risk factors for Stroke should be controlled, in order to prevent further cerebrovascular accidents.
2. Prevent stroke complications.
3. Specific pathology and patho-physiologies should be treated.[1]
4. Airway should be secured , breathing , circulation should be maintained.

5. Blood sugar should be maintained within normal limits.
6. Emergency non contrast Computed tomography films should be taken, since it helps to distinguish between ischemia and haemorrhage.
7. Points that favors Hemorrhagic stroke at that the time of presentation were Initial Maximum deficit, altered or diminished level of consciousness and increased blood pressure and the points that denotes Infarct were maximal at onset or remits after onset.[3]
8. Promotion of recovery of stroke patients.
9. Improve neurological function.

TREATMENT CATEGORIZATION [3]

1. Medical therapy
2. I.V. thrombolysis
3. Anti thrombotic treatment
4. Endovascular techniques
5. Neuroprotection
6. Stroke rehabilitation

Medical management

Aim of therapy:

To restore blood flow around ischemic penumbra.

1. I.V. Mannitol: Cerebral edema usually peaks around 2nd to 3rd day and it will last for 10 days, so I.V. Mannitol should be given in order to reduce cerebral edema. If it is not treated, it will result in herniation of the brain and finally it leads to sudden cardio-respiratory arrest and in such cases Hemi-craniotomy, where part of the skull can be removed temporarily.
2. Blood pressure monitoring and its reduction is necessary only when there is associated myocardial infarction, and the patient is planned for thrombolytic therapy (>185/110mmHg), Hypertensive emergencies.
3. Deep vein thrombosis prophylaxis should be given, by adding Subcutaneous Heparin (Unfractionated Heparin)
4. Heart rate reduction should be done with β1blocker Esmolol, which helps to restore maintain the mean arterial pressure to brain.
5. Hyperthermia should be treated with cooling blankets.
6. Blood sugar monitoring should be done since hyperglycemia results in poor outcome and it should be maintained around 110mgs/dL.[3]

I.V. Thrombolysis

Recombinant tissue plasminogen activator (rt-PA) is now used as a thrombolytic agent of choice. The incidence of intracranial haemorrhage is minimal with this drug. The time window period for administering rt-PA in

patients with ischemic stroke is 3 hours but it can be extended up to a maximum of 6 hours. The recommended dose of rt-PA is 0.9 mg /kg and the maximum dose of this drug is 90 mg. 10% of the drug should be given as i.v. bolus and remainder as intravenous infusion over a period of one hour. Frequent monitoring of blood pressure while administering this drug as infusion through large peripheral vein and infusion should be stopped once patient developed signs of neurological deficit and cryoprecipitate should be administered in such case. Urinary catheterization should be avoided for another 2 hours.[3]

Indications for thrombolysis

1. Clinical diagnosis of stroke should be made.
2. Patient should remain in the category of therapeutic window period of 3 hours.
3. There should not be any evidence of haemorrhage, edema, infarct involving more than 1/3 of involved infarct territory, mass effect, edema in CT scan.
4. Patient should be >18years.
5. Consent by patient attenders.[3]

Contra indications for thrombolysis

1. BP >185/110 mmHg inspite of treatment.
2. Patient having completed stroke in last 14 days or TIA symptomatalogy, and patient presenting with any upper and lower Gastrointestinal bleeding in previous 3 weeks, Recent myocardial infarction, Comatosed or stupor.
3. Platelets < 1 lakhs / cu.mm ; PCV < 25% ; Glucose <50 or >400 mgs /dL.
4. Heparin should not be used in preceding 48hours and elevated aPTT / INR .
5. Proir stroke or head trauma in last 90 days or prior intracranial haemorrhage.
6. When patient consciousness is lost (in comatosed state) or patient remaining in a stuporous condition.

ANTITHROMBOTIC TREATMENT

Platelet inhibition: Thrombaxane A2 is a prostaglandins, which is a platelet aggregator as well as vasoconstrictor. Aspirin acetylates the cyclooxygenase of platelets and completely inhibits the platelet plug formation .This platelet plug inhibition is irreversible. The anti-platelet activity of acetyl salicyclic acid will

remain for atleast 8 days. Low dose aspirin should be given as once daily dose. It will inhibit only thromboxane A2 production and the inhibition of prostacyclins is spared. So generally recommended dose for stroke is 50-325 mg/day.[3]

ANTICOAGULATION

Anticoagulation should be advised for all patients with atrial fibrillation which is due to non valvular heart disease and cardiac disease. Cerebral embolism can be prevented by maintaining an INR of 2-3. This anticoagulation can be brought out effectively by Vitamin K antagonists.

Indications for 3 month of anticoagulation

1. Left ventricular dysfunction
2. Atrial fibrillation
3. Anterior Q –wave infarction
4. Mural thrombus
5. Congestive cardiac failure

ENDOVASCULAR TECHNIQUES

Endovascular techniques should be planned for all patients for whom thrombolysis failed and contra-indications for thrombolysis exist .These candidates were eligible for endovascular mechanical thrombectomy. And by

this procedure, blood flow to the occluded vessels can be established within 8 hours of stroke.[3]

NEUROPROTECTION

These neuroprotective drugs will block the neuro- excitatory amino acid pathways and it promotes the tolerance of brain to ischemic effects. Some of the drugs which gives neuroprotection are Calcium Channel Antagonists (ex. Nimodipine , flunarizine,darodipine), Non competitive N-methyl–D-aspartate receptor antagonists (ex. dextromethorpan, eliprodil), Phosphatidyl choline synthesis (eg. Citicoline).[1]

STATINS

Statins are the inhibitors of 3-hydroxy -3 methylglutaryl coenenzyme A reductase inhibitor. These drugs were effective in reducing the cholesterol levels particularly low density lipoproteins. And it was found very effective in reducing the incidence of Coronary artery disease and cerebrovascular accidents. These statins has the following properties:

1. Normalizes the vascular endothelium
2. Reducing inflammation
3. Stabilizes the plaques mainly the central lipid core mass.

4. Reduces the platelet-fibrin thrombi and decreased white clots deposition on the endothelial surfaces.
5. Fibrous caps of atheromatous plaques get strengthened and stabilized.
6. Thrombogenicity of the atheromatous plaques gets decreased.[1]

STROKE REHABILITATION

- ✓ Speech therapy
- ✓ Occupational therapy
- ✓ Physical therapy
- ✓ Pharmacological therapy.[3]

ACUTE PHASE REACTANTS

In 1941, Avery and Theodore J Abernethy coined the term Acute Phase Reactants and also denoted that acutely ill patient's serum contains CRP.

Acute phase reactants are the markers of inflammation and they are elevated in inflammation, infection and they tend to appear or rise in the blood whenever the immune system comes in contact with proteins. This elevation of acute phase reactants indicates inflammatory burden and it gets elevated in vascular events.[19] Some of the acute phase reactants are

- ✓ α1 globulin
- ✓ α2 globulin

- ✓ α1anti trypsin
- ✓ Fibrinogen
- ✓ Fibrinonectin
- ✓ Serum Amyloid A protein
- ✓ Pre-Albumin
- ✓ Transferrin

Among these reactants, Pre-Albumin, Transferrin were negative phase reactants, they tend to decrease during inflammatory reactions whereas others increase during any inflammatory and infective conditions.[20]

Inflammation and CVA

The proposed mechanisms for role of inflammation in cerebrovascular disease are:

- ➢ Soon after an ischemic stroke, acute atherothrombotic event brings out an ischemic necrosis in acute cerebral infarction and brain damage.
- ➢ Formation of atheromatous plaques and fatty streaks (atherosclerosis) is a lifelong process.
- ➢ In Intracerebral hemorrhage, brain injury is delayed.
- ➢ Sub-Arachnoid hemorrhage causes vasospasm leading on to Cerebrovascular accidents.

HIGHLY SENSITIVE C-REACTIVE PROTEIN

C-reactive protein (CRP) is considered as an hallmark of the acute-phase response and seems to be a blood marker of inflammation. hsCRP is now considered as a marker of Atherosclerosis, and metabolic syndrome and helps to predicts cardiovascular events such as myocardial infarction, cerebrovascular accidents, peripheral arterial disease, sudden cardiac death.[21]

In 1930, Tillet and Francis discovered C-reactive protein (CRP), as a substance in serum sample of the patient, which is secreted in response to acute inflammation that reacted with C-polysaccharide of pneumococcus in Rockfeller hospital. This fraction was named as ' C ' Substance. Lofstrom noted non specific capsular swelling when few pneumococcal strains were mixed with patient's sera and noted that CRP gets elevated in infective, non-infective conditions, malignant neoplasms, cellular debris, tissue necrosis.

Synthesis and metabolism

CRP is synthesized mainly in liver. In both infectious, non-infectious conditions, the rate of synthesis and secretion of CRP are elevated under the influence of interleukins 1, interleukins 6, interleukins 17, Prostaglandins E, and Tumor necrosis Factor. The normal value of hsCRP is 3mg /L. Catabolism of CRP occurs in Liver, hence it was apparently removed from circulation and

the plasma half life is 19 hours, inspite of disease status. So CRP levels in Blood mainly depend on the rate of production. In Inflammatory conditions, these values get increased and doubles in every 8 hours and peaks around 36-50 hours. CRP concentration can may rises more than 500 mg/l which means, as much as a 1000-fold or more concentration change, in acute inflammatory states. The hsCRP is the lower concentration of normal CRP values, whereas the normal reference range of CRP is 0-8 mg/L.

Structure

CRP, belonging to pentraxin family, has a pentameric non-glycosylated polypeptide with covalent binding in between these proteins, arranged in cyclic pentameric symmetry, arranged in a disc like configuration with a central core. Human CRP has a molecular mass of 115,135 Da.

Functions of CRP

- Activator of Classical Complement Pathway and brings out endothelial dysfunction.
- Promotes opsonisation and it stimulates the procoagulant state.
- Decreases the release of platelets in acute inflammatory conditions.

- Increases the activity and motility of phagocytic cells.

Indications

1. Inflammatory conditions

- Rheumatoid Arthritis
- Reiter's syndrome
- Rheumatic fever
- Ankylosing spondylosis

2. Vascular causes

- Bechet syndrome,
- Polymyalgia rheumatic,
- Polyarteritis nodosa

3. Infective conditions

- Bacteial infections
- Viral infections
- Fungal infections
- Sepsis
- Pyogenic meningitis

- Intercurrent infections in leukemia

4. Screening test for different organic disease

5. To assess the prognosis and to predict the functional outcome of diseases in acute myocardial infarction, cerebrovascular accident.

6. In inflammatory conditions where CRP level is normal or not elevated are

- SLE
- Dermatomyositis
- Ulcerative colitis

HSCRP VALUES

HSCRP VALUES (MG/DL)	**INFERENCE**
0-1	LOW RISK
1-3	INTERMEDIATE RISK
>3	HIGH RISK

NATIONAL INSTITUTE OF HEALTH STROKE SCALE (NIHSS)

Neurological Examination stroke scale which has 15 items was designed by Thomas Brott in the year 1989, to know the impact of Acute Cerebral Infarction on neurological outcome and recovery. Due to its pit falls, it was modified later, to frame NIHSS.[24]

NIHSS will have a total score of 42. Patients with completed stroke, hemiplegia, hemianopia, hemineglect, Aphasia, facial palsy will have maximum score of 31.

1. Cranial Nerve/ Visual disturbances
2. Level of Consciousness
3. Motor weakness
4. Language/ Neglect – were the four important areas to be taken into account. Even based on this clinical parameter, scores can be computed and severity can be assessed.

Merits of NIHSS

- Helps in diagnosing Cerebrovascular accidents.
- To know the prognosis of stroke
- To determine functional disability
- Rapid way of assessing the patient, which can be done in 10 minutes.

Tested Item	Title	Response & Scores
1A	Level of Consciousness	0 – Patient is very alert 1 – Ready to fall asleep, lack of attention, patient will respond to painful stimuli 2 – Patient is not alert or oriented to time, person, place and remains in a state of confusion or frank delirium 3 – Patient is Comatosed and not responding to painful stimuli
1B	Orientation Questions	0 – Here patient answers correctly to 2 simple questions

		1 – Patient will answer 1 question correctly 2 – Patient will not answer correctly to any question
1C	Response to Commands	0 – Patient will do both work and task s perfectly 1 – Patient will do one task perfectly 2 – Patient will not do both tasks
2	Gaze	0 – Patient has normal horizontal movements 1 – Patient can have gaze palsy which is partial 2–Complete ophthalmoplegia
3	Field of vision	0 – Patients visual field is

		normal 1 – Patient will have Hemi-anopia which is partial 2 – Patient will have Hemi-anopia which is complete 3 – Here Hemi-anopia is bilateral
4	Facial Movements	0 – Normal 1 – Here facial palsy is subtle 2 – Patient will have facial weakness which is incomplete 3 – Here facial palsy is complete which is unilateral

5	Motor Functions (Arm) a) Left b) Right	0 – No fall when both forearms are stretched out and kept in supinated position 1 – Fall of forearm and hand occurs before 5 seconds 2 – Forearm and hands fall & supinate before 10 seconds 3 – No movement against gravity 4 – Total paralysis
6	Motor Functions (Leg) a) Left b) Right	0 – No drift 1 – Drift of leg oocurs before 5 seconds 2 – Fall of leg occurs even before 5 seconds

		3 – No movement against gravity 4 – Total paralysis
7	Limb Inco-ordination	0 – Normal 1 – Inco-ordination of only one limb 2 – Inco-ordination of two limbs
8	Sensory	0 – Patient will not have any sensory loss 1 – Here sensory loss is mild 2 – Here patient will have severe sensory loss
9	Language	0 – Patient can communicate and comprehend the language properly

		1 – Patient will have subtle loss of speech 2 – Patient will have severe loss of speech 3 – Patient will have both Broca & Wernicke's aphasia or mute
10	Articulation	0 – Normal 1 – Articulation defect is mild 2 – Articulation defect is severe
11	Extinction or inattention	0 – Absent 1 – One modality of sensation is loss 2 – Severe loss of sensation

Interpretation of NIHSS Score

0 – No stroke

1-4 – Minor stroke

5-15 – Moderate stroke

16-20 – Moderate to severe stroke

21-41 – Severe stroke

Modified Rankin Scale (MRS)

Dr. John Rankin designed Modified Rankin Scale in 1957, used to assess the clinical outcome and the neurological disability in stroke patients.

Parameters: MRS carries a total score of 0-6.

Score	Observations
0	Patient should not have any symptoms at all
1	Patient should not have any significant disability inspite of presence of symptoms and can able to perform routine daily normal activities
2	Patient will have slight disability and the person cannot perform all routine activities but manages to do his personal work without help

3	Patient is having moderate disability and needs some help, but able to walk without assistance
4	Patient will have moderately severe disability and cannot walk without help and unable to do his personal affairs without assistance
5	Here patient is having severe disability and the affected individual is bedridden, urinary incontinence will be present and needs continuous nursing care and attention
6	Dead

Studies supporting Stroke is an inflammatory process

Yusuf Tamam et al.[25], 2005 explain the role of acute phase proteins in acute stroke which is an inflammatory process. Here in this study, totally 53 patients were taken and age controlled subjects were also taken. Six APP (such as Haptoglobin, ceruloplasmin, hsCRP, fibrinogen, C3 and C4) were done on day 1, 3, 5 & 10. hsCRP, C3 and C4 levels were raised significantly on day 3, complements C3 and C4 on 5^{th} day and Haptoglobin on 10^{th} day. All these findings suggest stroke is an inflammatory process.

Studies supporting Stroke is an inflammatory process

Study	Year of study done
Muir et al.[26]	1999
Leiden 85 plus study	2002
Eikelboom et al.[28]	2003
Yusuf tamam et al.[25]	2005

Prognostic significance of hsCRP in Acute Ischemic Stroke

In Muir et al.26228 cases of ischemic stroke were taken and was followed for a period of 950 days. Geometric mean CRP concentration was 10.1 mg / L. Mortality rate was more in patients with CRP > 10.1 mg/l than other group of patients with CRP ≤10.1 mg / L. These studies reveal that inflammation play a role in Acute Ischemic Stroke and also higher CRP predicts future Cardiovascular mortality.

In Bergen Stroke Study,[34] CRP & NIHSS were measured in 498 patients with ischemic stroke within 24 hours of onset. NIHSS and CRP levels were seen while admitting the patient. CRP cut off of 3 mg/l was made. Recovery is measured using MRS & Barthel Index. Patients with high CRP along with high NIHSS (p=0.01) had long term mortality (p=0.0002). Patients with high

CRP also had poor functional recovery and outcome. (MRS > 3, BI < 95) with p values as p =0.01 & p = 0.03.

John W Eikelboom et al., a case control study stroke cases (202) were identified from 199 hospitals and blood samples were drawn for CRP and patients with higher CRP values (8.50) correlate with stroke severity assessment by Oxford Handicap Scale score (p=0.03) and Barthel index (p=0.001). From these results the author concludes that there was an independent relationship between high CRP value and Ischemic stroke.

Relationship between hsCRP and clinical functional outcome after acute ischemic stroke in a Korean population was studied. In this study, hsCRP levels were taken within 24 hours and on 7^{th} day of onset in 417 Korean patients. MRS scanning was done after 12 months and hsCRP concentation got correlated significantly with MRS score.

In Hamidon et.al. 2004, Prognostic significance of CRP values in CVA patients were studied. For all ischemic stroke patients (about 84 patients) joined between May 2002 – July 2002 in Hospital University, Kebargsaan, Malaysia, hsCRP was taken. After one month, Barthal Index was used to know the function disability. About 29 patients who had elevated CRP had severe functional disability and also patient had larger infarct.

In study conducted by Mario Di Napolis 2001, prognostic value of hsCRP in acute ischemic stroke was studied. Hundred and ninty three patients were chosen and hsCRP levels were taken on admission and at the time of discharge. From receiver operator curve, CRP cut off of 1.5 mg/l which provides optimum senstivity and specificity was made. Admission CRP (Hazard ratio 2.78 p= 0.0021) and discharge CRP (Hazard ratio 9.42, $p<0.0001$) was also obtained. This study reveals discharge CRP was considered as the strongest independent marker of future worse outcome (in terms of cardio vascular mortality).

MATERIALS AND METHODS

SETTING:

Patients admitted in medical ward, Government Rajaji Hospital, Madurai

COLABORATIVE DEPARTMENTS:

Department of Biochemistry, Neurology, Radiology, Medicine, Madurai Medical College, Madurai.

STUDY DESIGN:

Prospective cross sectional observation study

PERIOD OF STUDY:

March 2012 to October 2012

STUDY POPULATION:

50 Acute ischemic stroke patients admitted in medical ward, Government Rajaji Hospital, Madurai.

DEFINITIONS FOLLOWED IN THIS STUDY:

STROKE:

As per WHO criteria, Acute Stroke is defined as “rapidly developing focal or generalized (for coma patients) neurological alterations in cerebral function with signs and symptoms lasting for more than 24 hours or leading on to death, without any apparent cause for stroke except vascular etiology.

HYPERTENSION:

Hypertension was defined as patients with previous record of atleast 2 recordings of >140 / 90 mmHg or patients who are on regular intake of anti hypertensive medications.

DIABETES:

Diabetes was defined as patients with Random Blood Sugar of >200mg/dL, Fasting blood sugar of >126 mg/dL, Post prandial blood sugar of >200mg/dL or patients who are in need of regular intake of anti-diabetic drugs.

DYSLIPIDEMIA:

Dyslipidemia was defined as patients with Fasting Serum Cholesterol values of more than 220 mgs/dL.

HSCRP:

Immunoturbidity method was adopted to find hsCRP values. HsCRP cut-off value of 3 mg /dL was made.These HsCRP values were correlated with NIHSS score at the admission and MODIFIED RANKIN SCALE score which denotes the functional recovery of the patient after 4 weeks. Patients with elevated HsCRP will have high NIHSS score which denotes the severity and high MRS score which denotes the poor outcome.

NIHSS SCORE

NIHSS scoring was made based on the clinical parameters. In this study, patients with a score of 1- 4 were considered as MILD, 5-15 were considered as MODERATE, >15 were considered as SEVERE category.

INCLUSION CRITERIA:

1. All patients with new onset focal neurological deficit following ischemic stroke, presented within 48 hours of onset of stroke are taken into study.
2. Patients >14 years and of both sexes are included in the study.
3. Patients with new onset stroke with past history of hypertension, diabetes mellitus, dyslipidemeia, smoking, alcohol were included.

EXCLUSION CRITERIA:

1. Patients with age more than 80 years were excluded.
2. Patients with malignancy and clinical findings and blood investigations suggestive of infection were excluded.
3. Individuals with Connective Tissue disorders and Rheumatic heart disease, Coronary Artery disease were excluded.
4. Patients with prior history of transient ischemic attacks or reversible ischemic neurological deficit, cerebrovascular accidents were excluded.

5. Patients with features of haemorrhage such as sub-dural haemorrhage, sub-arachnoid haemorrhage, and intracerebral haemorrhage were excluded with the aid of CT scan.

6. History of recent surgery and trauma.

7. CNS tumors.

ETHICAL CLEARANCE:

Necessary ethical clearance was obtained from ethical committee, Government Rajai Hospital, Madurai.

STUDY METHODS:

50 patients who had acute ischemic stroke were taken for study. Those patients who got admitted within 48 hours of onset of stroke were only included in this study. As soon as patient got admitted, verbal consent was obtained from patient or attenders. Then complete and relevant medical history, complete neurological examination, routine blood and radiological investigations were done and all data were recorded in a standardized proforma.

CT scan was taken to exclude the haemorrhagic stroke and to identify the site or territory of infarct. Serum hsCRP level were taken as soon as patient got admitted in the hospital. National Institute of Health Stroke Scale (NIHSS)

scoring was applied at the time of admission and these patients were categorized as mild, moderate and severe groups.

This acute ischemic stroke patients were treated according to standard treatment protocols and in the study, and the patients were treated with Aspirin, Atorvastatin, physiotherapy and supportive care. None of the patients in the study group were thrombolysed. Anti edema measures were adopted with either intravenous Mannitol or oral Glycerol. Modified Rankin Scale was applied to know the functional recovery of the patient after 4 weeks when patient is on follow up and attending the review op. MRS score of 3,4,5,6 were included under Poor Outcome and scores of 1,2 were considered as Good outcome.

STATISCAL METHODS

All the collected data were computed in Master chart. Statiscal data analysis was done. Chi Square test, Means, Standard deviation, ‘p’ values were calculated. A ‘p’ value less than 0.05 denotes significant relationship. Pearson’s r correlation test and scatter plot analysis were also done for given data.

RESULTS AND ANALYSIS

SEX DISTRIBUTION

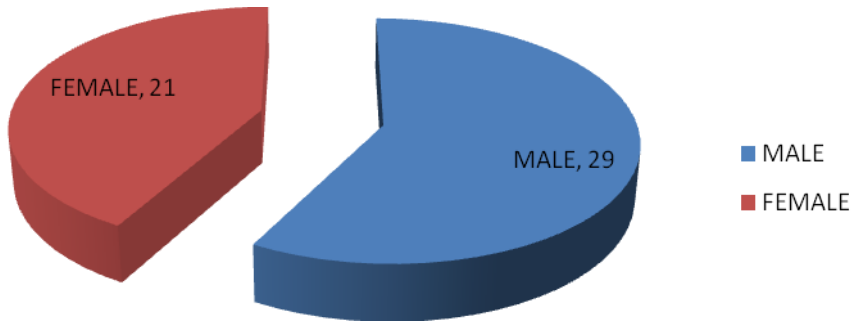
Total number of patients included in the study = 50 (100%)

Number of Male cases included in the study = 29 (58%)

Number of Female cases included in the study = 21 (42%)

TABLE 1 SEX DISTRIBUTION

SEX	NO.OF CASES	PERCENTAGE
MALE	29	58%
FEMALE	21	42%
TOTAL	50	100%



SEX VS hsCRP

Out of 29 male patients , Number of male patients who had hsCRP values < 3 mg/L are 14 (48.3 %) and the number of male patients who had hsCRP values ≥ 3 mg / L are 15 (51.7%).

And out of 21 female patients , 8 (38.1 %) female cases had hsCRP values < 3 mg / L and 13 (61.9 %) female patients had hsCRP level ≥ 3 mg/ L .

TABLE 2 SEX VS hsCRP

SEX	NO.OF PATIENTS	HsCR P (mg/L)		TOTAL
		<3	≥ 3	
MALE	COUNT	14	15	29
	%	48.3%	51.7%	100.0%
FEMALE	COUNT	8	13	21
	%	38.1%	61.9%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0 .474 NOT SIGNIFICANT

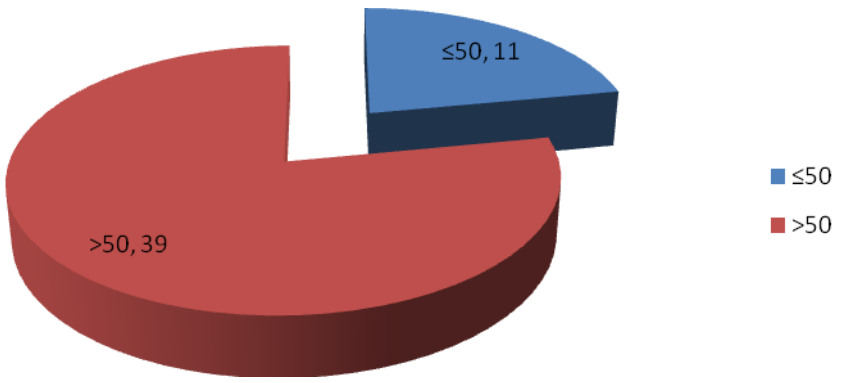
The correlation between sex and hsCRP was statistically not significant.

AGE DISTRIBUTION

Out of 50 patients, 11(22%) patients were in the age group of ≤ 50 years and 39 (78%)patients were in the age group of > 50 years.

TABLE 3 AGE DISTRIBUTION

AGE (IN YEARS)	NO.OF PATIENTS
≤ 50	11
> 50	39
TOTAL	50



AGE VS hsCRP

Out of 11 (22%) patients who were in the age group of ≤ 50 years, 6 (54.5%) patients had hsCRP < 3 mg/L and 5 (45.5%)patients had hsCRP ≥3 mg/L.

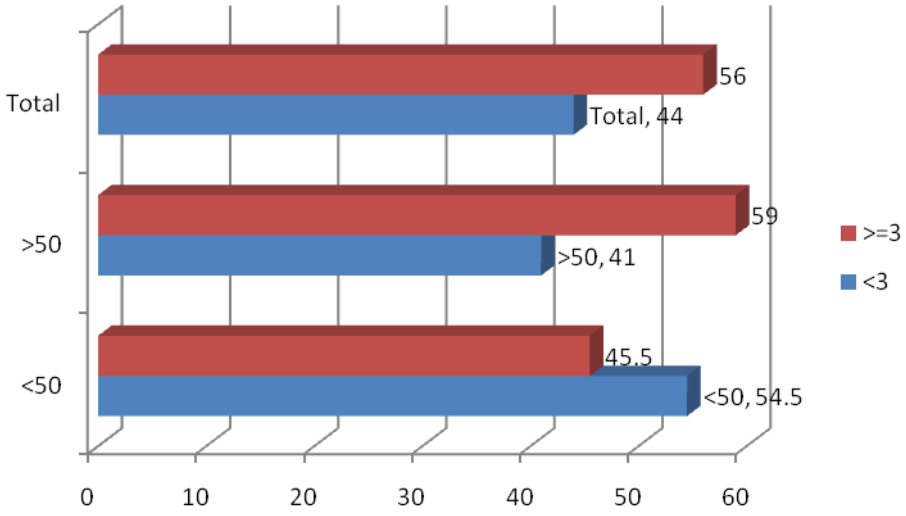
Out of 39 (78%) patients who were in the age group of > 50 years, 16 (41%) patients had hsCRP < 3 mg/L and 23 (59%) patients had hsCRP ≥3 mg/L.

TABLE 4 AGE VS hsCRP

AGE (IN YEARS)	NO. OF PATIENTS	hsCRP (mg/L)		TOTAL
		<3	≥3	
≤50	COUNT	6	5	11
	%	54.5%	45.5%	100.0%
>50	COUNT	16	23	39
	%	41.0%	59.0%	100.0%
Total	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0.503 NOT SIGNIFICANT

The correlation of Age with hsCRP was statistically insignificant.



SMOKERS VS hsCRP

HsCRP profile was done in all 50 cases which includes both smokers and non smokers .Out of 28 patients who are all non smokers , 12 (42.9%) patients had hsCRP < 3 mg / L and 16 (57.1%) patients had hsCRP ≥3 mg/L .

Out of 22 patients, who are all smoking, 10 (45.5 %) patients had hsCRP < 3 mg / L and 12 (54.5 %) patients had hsCRP ≥3 mg/L .

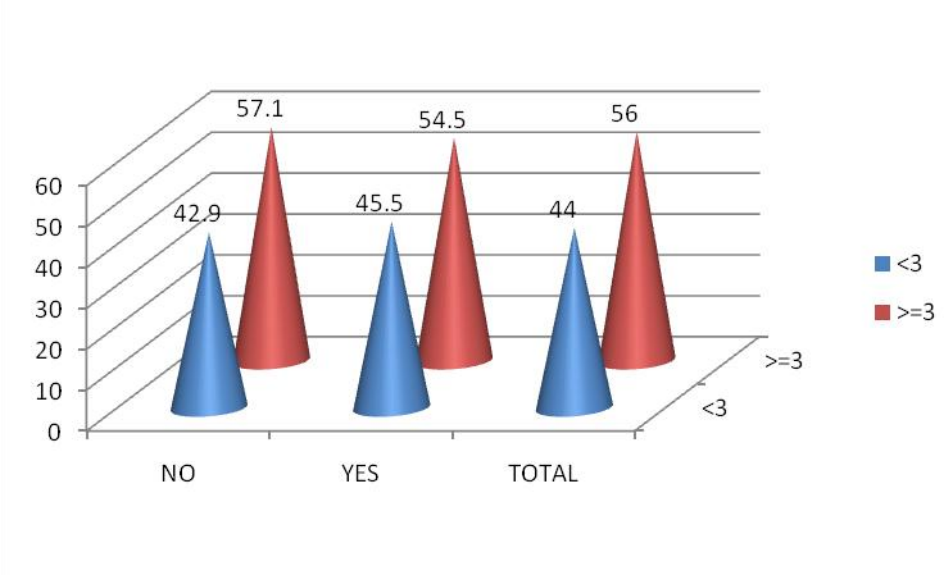
TABLE 6 SMOKERS VS hsCRP

SMOKING	NO.OF PATIENTS	hsCRP(mg/L)		TOTAL
		<3	≥3	
NO	COUNT	12	16	28
	%	42.9%	57.1%	100.0%

YES	COUNT	10	12	22
	%	45.5%	54.5%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0 .854 NOT SIGNIFICANT

The correlation between smokers and hsCRP was statiscally not significant.



ALCOHOLICS Vs hsCRP

In both alcoholics and non alcoholics, hsCRP profile was done. The number of patients with hsCRP < 3 mg / L were 14 (48.3%) and hsCRP ≥3 mg / L were 15 (51.7%) among total 29 patients who were non alcoholics.

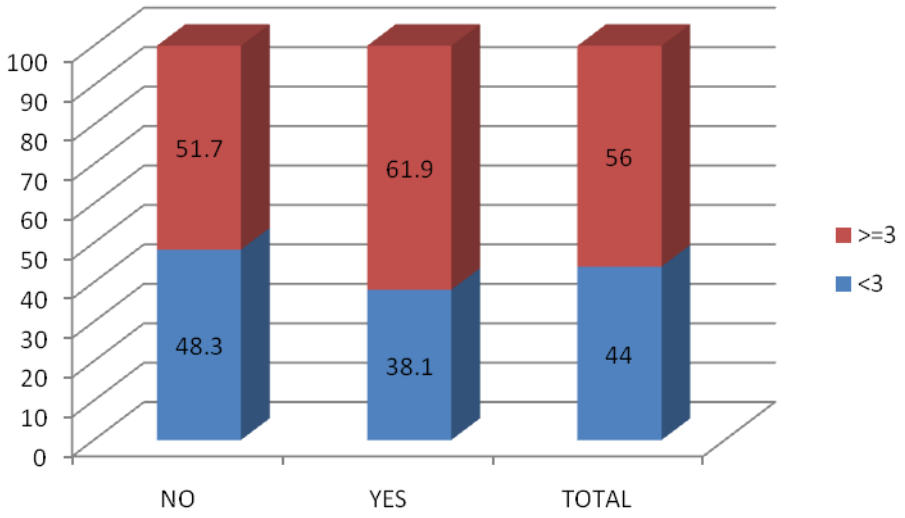
The number of patients with hsCRP < 3 mg / L were 8 (38.1%) and hsCRP ≥3 mg / L were 13 (61.9%) among total 21 patients who were alcoholics .

TABLE 7 ALCOHOLICS Vs hsCRP

ALCOHOL	NO.OF PATIENTS	hsCRP (mg/ L)		TOTAL
		<3	≥3	
NO	COUNT	14	15	29
	%	48.3%	51.7%	100.0%
YES	COUNT	8	13	21
	%	38.1%	61.9%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0.474 NOT SIGNIFICANT

The correlation between hsCRP and Alcoholics was statistically insignificant



DIABETICS Vs hsCRP

hsCRP values were correlated with both diabetics and non diabetics patients. Among 11 non diabetics, 9 (81.8%) patients had hsCRP <3 mg / L and 2 (18.2%) patients had hsCRP ≥ 3 mg / L .

Among 39 diabetics, the number of patients with hsCRP <3 mg / L were 13 (33.3%) and with hsCRP ≥ 3 mg / L were 26 (66.7%).

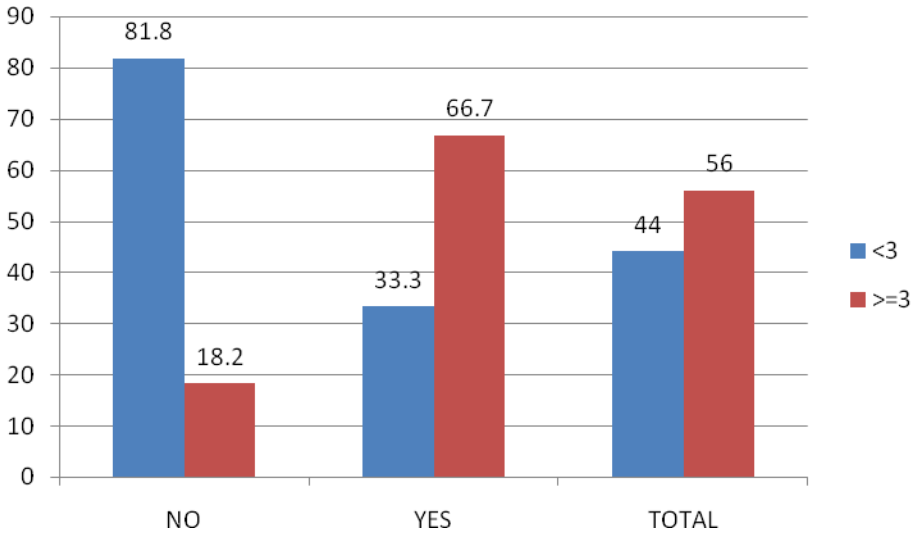
TABLE 8 DIABETICS Vs hsCRP

DIABETES	NO.OF PATIENTS	hsCRP(mg / L)		TOTAL
		<3	≥3	
NO	COUNT	9	2	11

	%	81.8%	18.2%	100.0%
YES	COUNT	13	26	39
	%	33.3%	66.7%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0 .006 SIGNIFICANT

The correlation between hsCRP and Diabetes was significant statistically.



HYPERTENSION Vs hsCRP

hsCRP values were correlated in both hypertensives and non hypertensives patients. Out of 31 non hypertensive patients, 18 (58.1%) patients had hsCRP <3 mg / L and 13 (41.9%) patients had hsCRP ≥ 3 mg / L .

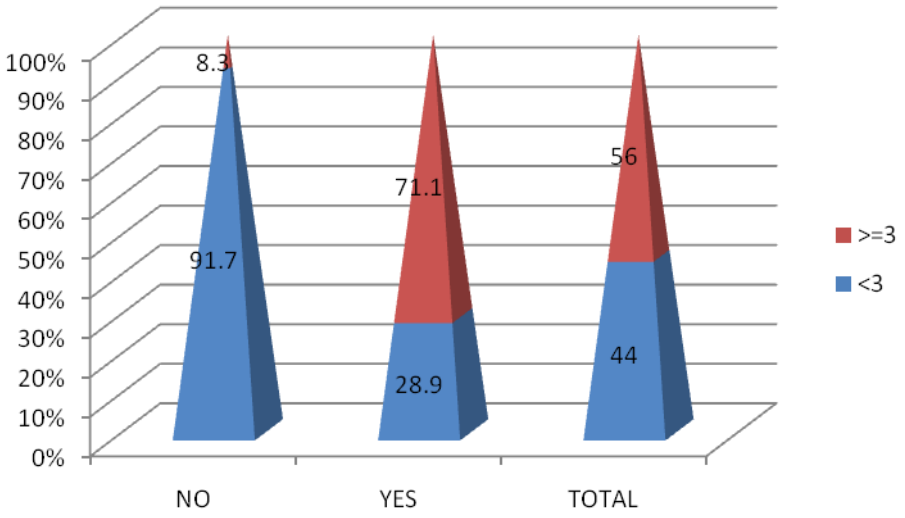
Out of 19 hypertensive patients, 4 (21.1%) patients had hsCRP <3 mg / L and 15 (78.9%) patients had hsCRP ≥ 3 mg / L.

TABLE 9 HYPERTENSION Vs hsCRP

HTN	NO.OF PATIENTS	hsCRP (mg/L)		TOTAL
		<3	≥ 3	
NO	COUNT	18	13	31
	%	58.1%	41.9%	100.0%
YES	COUNT	4	15	19
	%	21.1%	78.9%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = .010 SIGNIFICANT

The correlation between hsCRP and Hypertensives was statistically significant.



CHOLESTEROL vs hsCRP

hsCRP profile was seen in both dyslipidemic and non dyslipidemic patients . Among 12 non dyslipidemic patients, 11(91.7%) had hsCRP <3 mg / L and 1(8.3%) patients had hsCRP ≥ 3 mg / L.

Among 38 dyslipidemic patients, 11(28.9%) had hsCRP <3 mg / L and 27(71.1%) patients had hsCRP ≥ 3 mg / L.

TABLE 10 CHOLESTEROL vs hsCRP

CHOLESETEROL	NO.OF PATIENTS	hsCRP(mg/L)		TOTAL
		<3	≥3	
NO	COUNT	11	1	12
	%	91.7%	8.3%	100.0%

YES	COUNT	11	27	38
	%	28.9%	71.1%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

P value = 0 .000 SIGNIFICANT

The correlation between hsCRP and Dyslipidemic patients was statistically significant.

LOSS OF CONSCIOUSNESS Vs hsCRP

In Patients with loss of consciousness, hsCRP profile was done. The number of patients with hsCRP < 3 mg /L were 21 (58.3%) and hsCRP ≥ 3 mg / L were 15 (41.7%) among conscious patients.

The number of patients with hsCRP < 3 mg /L were 1 (7.1%) and hsCRP ≥ 3 mg / L were 13 (92.9%) among un-conscious patients.

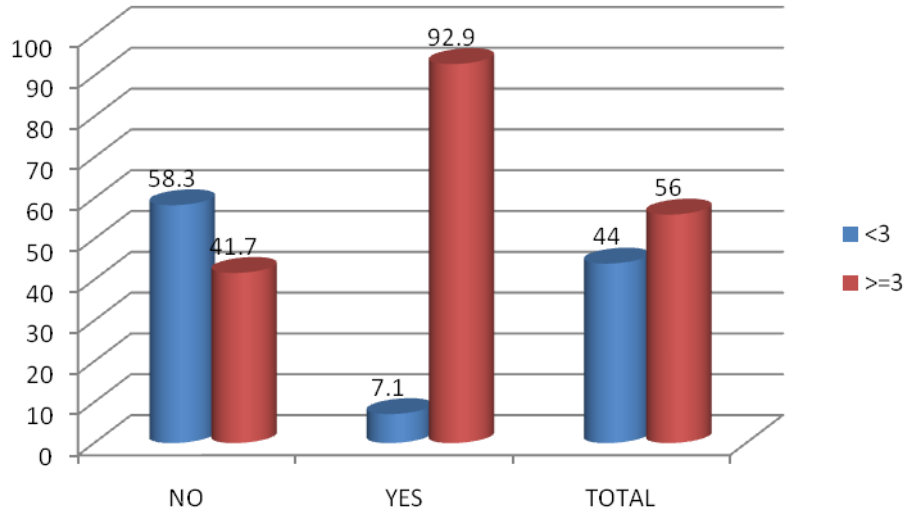
TABLE 11 LOSS OF CONSCIOUSNESS Vs hsCRP

LOC	NO.OF PATIENTS	hsCRP(mg/L)		TOTAL
		<3	≥3	
NO	COUNT	21	15	36
	%	58.3%	41.7%	100.0%

YES	COUNT	1	13	14
	%	7.1%	92.9%	100.0%
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0 .001 SIGNIFICANT

The correlation between hsCRP and Unconscious patients was statistically significant.



INFARCT TERRITORY vs hsCRP

HsCRP profile was done in patients with various territory of infarct in ct brain.

Among ACA territory infarct patients, 7 (70.0%) patients had hsCRP < 3 mg /L and 3 (30.0%) had hsCRP ≥ 3 mg / L .

Among MCA territory infarct patients, 6 (20.7%) patients had hsCRP < 3 mg /L and 23 (79.3%) had hsCRP ≥ 3 mg / L.

Among PCA territory infarct patients, 2 (100.0%) patients had hsCRP < 3 mg /L and 0 patients had hsCRP ≥ 3 mg / L.

Among others category which includes patients with watershed infarct and lacunar infarct in their CT films, 7(77.8%) patients had hsCRP mg / L > 3 mg/L and 2 (22.2%) had hsCRP ≥ 3 mg / L.

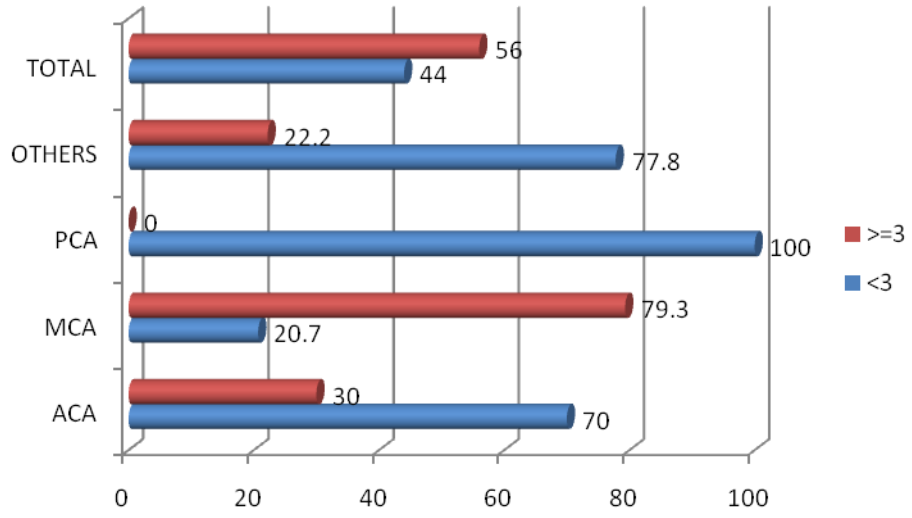
TABLE 12 INFARCT TERRITORY vs hsCRP

INFARCT TERRITORY	NO OF PATIENTS	hsCRP(mg/L)		TOTAL
		<3	≥3	
ACA	COUNT	7	3	10
	%	70.0%	30.0%	100.0%
MCA	COUNT	6	23	29
	%	20.7%	79.3%	100.0%
PCA	COUNT	2	0	2
	%	100.0%	0.0%	100.0%
OTHERS(WATERSHED INFARCT, LACUNAR	COUNT	7	2	9
	%	77.8%	22.2%	100.0%

INFARCT)				
TOTAL	COUNT	22	28	50
	%	44.0%	56.0%	100.0%

p value = 0 .001 SIGNIFICANT

The correlation between hsCRP and various territory of infarct in CT scan was statistically significant.



DESCRIPTIVE STATISTICS

The maximum and minimum mean values of hsCRP in the study are 6.9 and 1.2 with an average mean of 3.544.

The maximum and minimum mean values for NIHSS scoring system in the study is 33 and 5, with an average mean of 13.78

The maximum and minimum mean values for MRS scoring system in the study is 6 and 1, with an average mean of 3.16.

From this, it is evident that patients with a minimum hsCRP mean value of 1.2 had

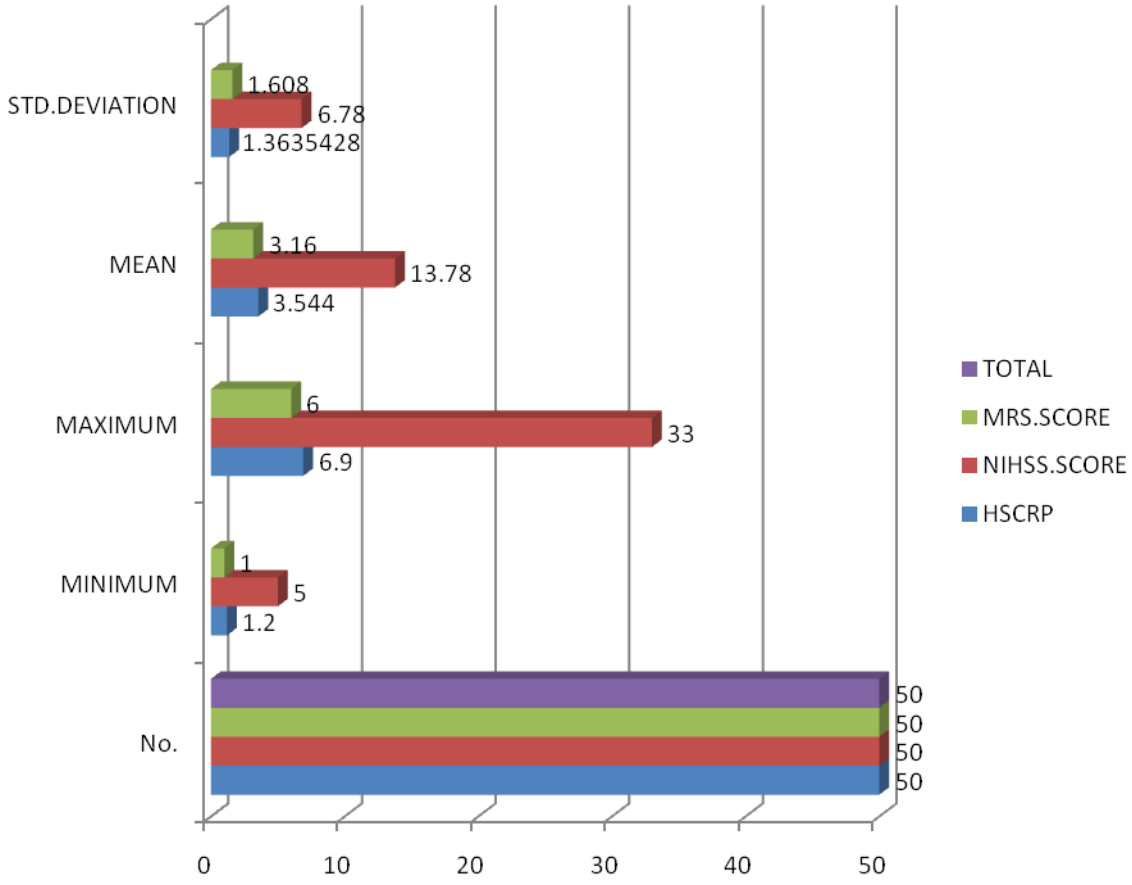
a) NIHSS score minimum mean value of 5 which comes under moderate group and
b) MRS minimum mean value of 1 which comes under good outcome.

And patients with hsCRP maximum mean value of 6.9 had

a) NIHSS maximum mean value of 33 which comes under severe category
b) MRS maximum mean value of 6 which comes under poor outcome.

TABLE 13 DESCRIPTIVE STATISTICS

VARIABLES	No.	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
HSCRP	50	1.2000	6.9000	3.544000	1.3635428
NIHSS.SCORE	50	5	33	13.78	6.780
MRS.SCORE	50	1	6	3.16	1.608



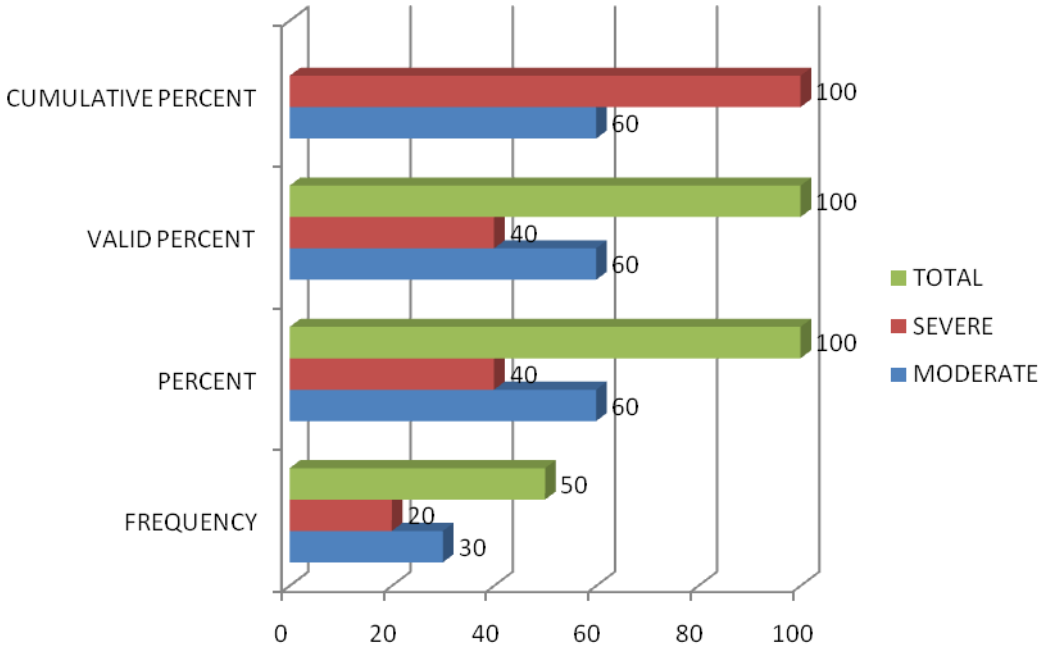
NIHSS DESCRIPTIVE STATISTICS

Out of total 50 acute ischemic stroke cases, 30 (60%) patients comes under severity group of *moderate* under NIHSS scoring system.

And 20 (40%) patients comes under severity group of *severe* under NIHSS scoring system.

TABLE 14 NIHSS DESCRIPTIVE STATISTICS

NIHSS	FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
MODERATE	30	60.0	60.0	60.0
SEVERE	20	40.0	40.0	100.0
TOTAL	50	100.0	100.0	00.0



HSCRP VS NIHSS

HsCRP profile was done in all patients and it was summated with various scoring categories of NIHSS.

Out of 30 cases who comes under moderate category in NIHSS , 22 (73.33%) cases had hsCRP values < 3mg / L and 8 (26.67) cases had hsCRP values ≥ 3 mg / L.

Out of 20 cases who were under severe category in NIHSS, no cases had hsCRP values < 3mg / L and 20 (100%) cases had hsCRP values ≥ 3 mg/L.

TABLE 15 HSCRP VS NIHSS

NIHSS	NO.OF PATIENTS	hsCRP(MG/L)		TOTAL
		<3	≥3	
MILD	COUNT	0	0	0
	%	00.00	00	00
MODERATE	COUNT	22	8	30
	%	73.33	26.67	100
SEVERE	COUNT	0	20	20
	%	00.00	100	100
TOTAL	COUNT	22	28	50
	%	44	56	100

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS

This table denotes strong correlation between hsCRP and NIHSS score. Change in hsCRP values strongly correlates with change in NIHSS scores.

There is also positive correlation between NIHSS score and HSCRP values, that is any increase in HSCRP will increase NIHSS scores and decrease in HSCRP values will decrease NIHSS scores.

TABLE 16 HSCRP VS NIHSS

hsCRP	PEARSON CORRELATION	1	**.844**
	P VALUE		**.000**
	N	50	50
NIHSS	PEARSON CORRELATION	.844	1
	P VALUE	.000	
	N	50	50

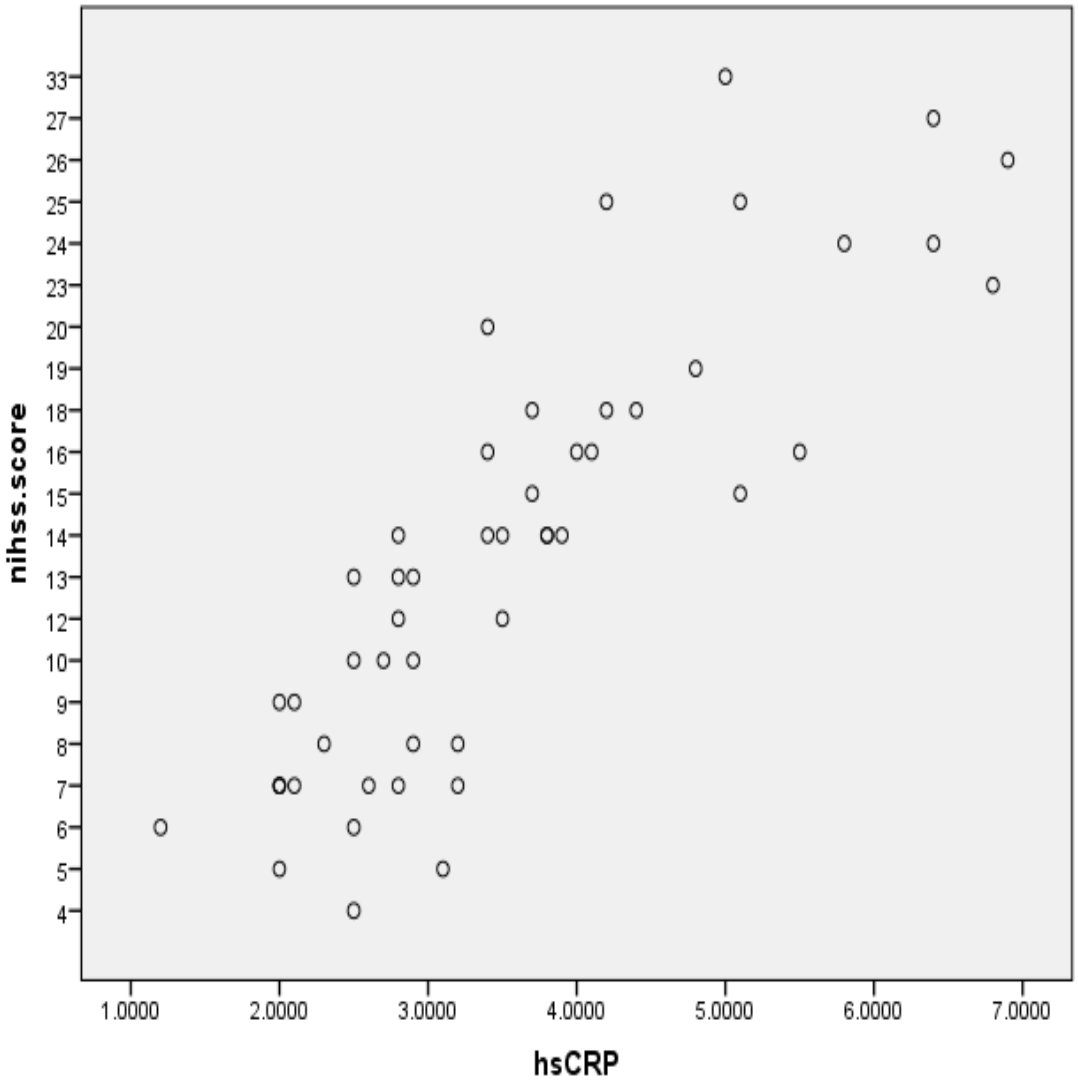
P =0.000 SIGNIFICANT

The correlation between hsCRP and NIHSS was stastically significant.

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS

Scatterplot analysis reveals that there is a positive correlation between HSCRP values and NIHSS scores. Increase in HSCRP increases with NIHSS scores.

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS BETWEEN hsCRP VALUES AND NIHSS SCORES

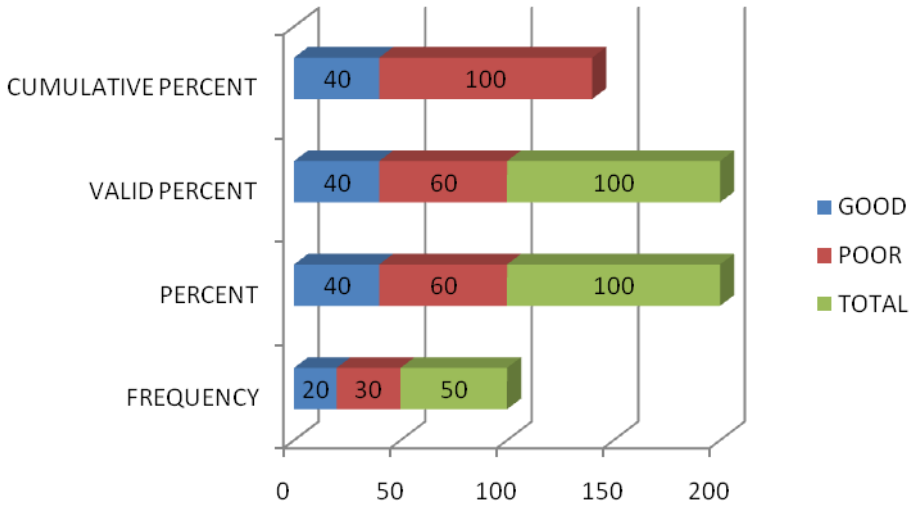


MODIFIED RANKIN SCALE

Among 50 total cases of stroke, 20 (40%) patients comes under good outcome by MRS scoring system and 30 (60%) patients comes under poor outcome by MRS scoring system.

TABLE 17 MODIFIED RANKIN SCALE DESCRIPTIVE STATISTICS

MRS	FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
GOOD	20	40.0	40.0	40.0
POOR	30	60.0	60.0	100.0
TOTAL	50	100.0	100.0	



hsCRP VS MODIFIED RANKIN SCALE

hsCRP values were correlated with various outcomes in Modified Rankin Scale.

Among 20 good outcome patients, 16 (80%) cases had hsCRP values < 3mg / L and 4 (20%) cases had hsCRP values ≥ 3 mg / L .

Among 30 poor outcome patients, 6 (20%) cases had hsCRP values < 3mg / L and 24 (80%) cases had hsCRP values ≥ 3 mg / L.

TABLE 18 hsCRP VS MODIFIED RANKIN SCALE

MRS	NO.OF PATIENTS	hsCRP(MG/L)		TOTAL
		<3	≥3	
GOOD	COUNT	16	4	20
	%	80	20	100
POOR	COUNT	6	24	30
	%	20	80	100
TOTAL	COUNT	22	28	50
	%	44	56	100

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS

This table denotes strong correlation between hsCRP and MRS score. Change in hsCRP values strongly correlates with change in MRS scores.

There is also positive correlation between MRS score and hsCRP values, that is any increase in hsCRP will increase MRS scores and decrease in hsCRP values will decrease MRS scores.

TABLE 19 hsCRP VS MODIFIED RANKIN SCALE

		hsCRP(MG/L)	MRS-SCORE
hsCRP	PEARSON CORRELATION	1	**.900**
	P VALUE		**.000**
	N	50	50
MRS SCORE	PEARSON CORRELATION	.900**	1
	P VALUE	.000	
	N	50	50

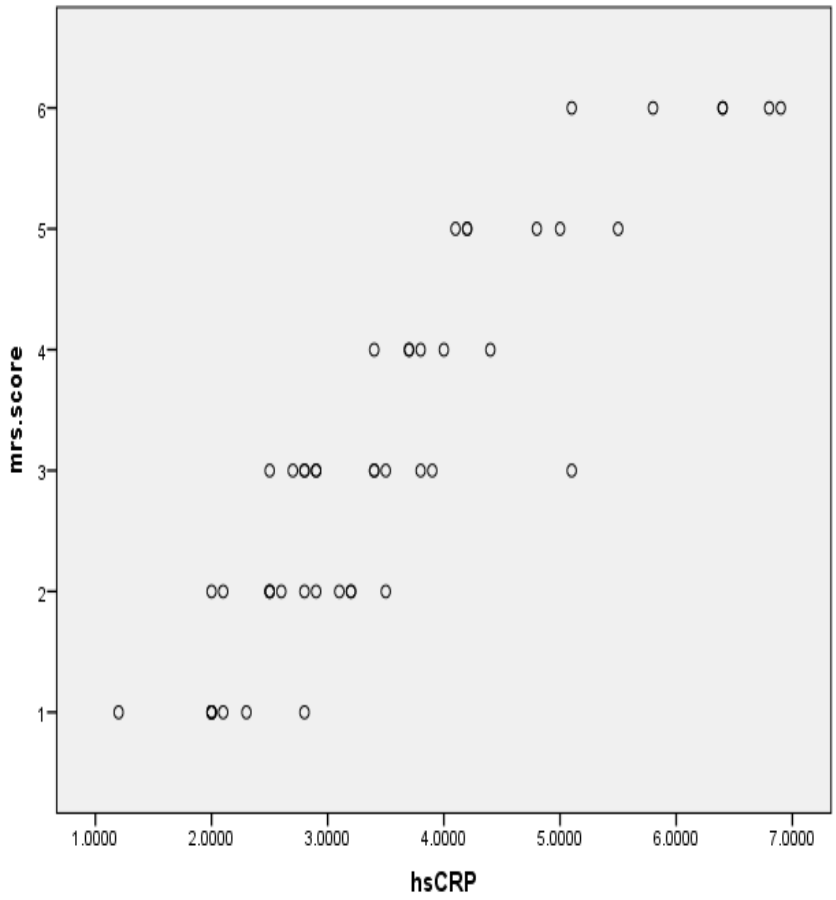
p value = .000 SIGNIFICANT

The correlation between hsCRP and MRS scale was statistically significant.

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS

Scatterplot analysis reveals that there is a positive correlation between hsCRP values and MRS scores .Increase in hsCRP increases with MRS scores.

PEARSON'S r CORRELATION AND SCATTER PLOT ANALYSIS BETWEEN hsCRP VALUES AND MRS SCORES



DISCUSSION

Stroke is now considered as a major consequence of cerebrovascular accidents and health hazard to the society. In this study of prognostic significance of hsCRP in Acute Ischemic Stroke consists of a group of 50 patients who were admitted in Government Rajaji Hospital from March 2012 to October 2012. In this study, hsCRP was taken within 48 hrs and NIHSS scoring was applied on the day of admission. Totally 50 cases were included in the study. Among the 50 cases included in this study 28 cases (56%) had hsCRP values ≥ 3 mg/l and 22 cases (44%) had hsCRP < 3 mg/l.

Number of patients died in this group is 6. All these patients had a hsCRP of ≥ 3 mg/l.

Out of these 28 cases who has hsCRP ≥ 3 mg/l, 26.67% of cases comes under moderately severe category and 73.33% cases comes under severe category. On the other hand, among the remaining 22 cases who had hsCRP <3mg/l, all the 22 cases comes under moderately severe and none in severe group.

Pearson's r correlation also reveals the strong correlation between hsCRP and NIHSS scores. Pearson's r value is 0.844 which is close to one. A

positive correlation exists between these 2 variables with a 'p' value of 0.00, which is statistically significant.

Scatter plot analysis reveals the positive correlation between hsCRP & NIHSS. Any increase or decrease in hsCRP score analogous linearly with increase/decrease severity score of NIHSS.

Out of 28 cases with hsCRP ≥3 mg/l 4 cases were in good outcome category and 24 cases in poor outcome category of MRS scores.

In contrast among 22 cases with hsCRP < 3 mg/l, 16 cases were in good outcome and 6 cases were in poor outcome category in MRS Score. Pearson's r correlation analysis reveals strong as well as positive correlation between hsCRP and MRS. Pearson's r value is 0.900 which is close to 1 and is positive variable. So any increase in hsCRP will favour the poor outcome of patients in terms of death and severe disability.

Studies favoring Prognostic Significance of hsCRP in Acute Ischemic Stroke

S.No	**Studies**	**Year**
1.	Muir et al.[26]	1993
2.	Bocola V, Papa F et al.[32]	2001
3.	Di Napoli M et al.[30]	2001,2005, 2009

4.	Wirnbeck et al.[29]	2002
5.	John W. Erkel boem et al.[27]	2003
6.	Hamidon et al.[31]	2004
7.	Alessandro terruzzi et al.	2008
8.	Bergen Stroke Study[34]	2009
9.	Rahman KM et al.[33]	2011
10.	Arenillas et al.[28]	2012

Sex

In the present study, Incidence of stroke patient in male is 58% whereas in female patients it is 42%. This incidence data was supported by Thomas Kuruvill et al.[35] in which males has higher incidence than female and in younger age group. No significant relationship exists between Sex and hsCRP in the present study, which was supported by Y.Tamam et al. 2005.

Age

In the present study, incidence of stroke is more common among patient with the age group of more than 50 years. And also hsCRP values are elevated in this age group, but it is not statistically significant. This was supported by Juan F. Arenillas et al. 2003.

Smoking

Smoking and Alcohol was not statistically significant. This result is against the findings of Dahovska et al.[36]The small sample value (only 50 cases considered) may be the reason for this contradiction.

Studies which shows hsCRP is not statiscally significant in relation to hsCRP.

S.No	Study	Year
1	Juan F.Arenillas	2003
2	Y.Tamam et al.	2005

Diabetes

In this present study, there is significant correlation between hsCRP and diabetes with a p-value of 0.006. This was supported by number of studies.

Studies in favor of rise in blood sugar increases hsCRP level

S.No	Study	Year
1	Guo et al.	2003
2	Paul M. Ridker et al.[37]	2003
3	Bergen Stroke Study	2009

Hypertension

In this present study, there is a significant correlation between hsCRP and Hypertension with a p value of 0.01. These findings are in agreement with following studies conducted by Xu T., Liu y.et al.[38] in 2008 and Nadir Rifai et al. in 2005.

Cholesterol

In the present study, there is a significant correlation between hsCRP and Serum Cholesterol level with a p value of 0.00. This findings were similar and in concordance with Cesari et al.[39] 2003 and Ridker et al. in 200.[40]

Infarct territory

In this present study, there is a significant correlation between infarct and hsCRP with a p value of 0.001. This reveals close association between Atherosclerosis and occurrence of newer ischemic events, which are caused by large occlusion of large intracranial vessels. This was supported by Arenillas et al. in 2003.

This study demonstrates the prognostic significance of hsCRP in acute ischemic stroke patients in correlation with stroke scores, which were measured at the time of admission (NIHSS) and four weeks after discharge (MRS).

This study also demonstrates the significant correlation between hsCRP and cordiovascular risk factors such as diabetes, hypertension, and cholesterol level. Stroke is common in this risk groups and had significantly higher hsCRP.

CONCLUSION

- ✓ This present study is a cross sectional observation study of prognostic significance of highly sensitive C-reactive protein in acute ischemic stroke patients.
- ✓ The present study shows male predominance with majority of patients in the age group of greater than 50 years.
- ✓ The present study revealed significant association between hsCRP and Diabetes Mellitus, Hypertension & Cholesterol level.
- ✓ This study demonstrates the significant rise in hsCRP in ischemic stroke patients in correlation with high scores with NIHSS which indicates the severity.
- ✓ This study reveals the poor outcome in correlation with high hsCRP values and good outcome in correlation with low hsCRP values.
- ✓ This study also explains statistically significant relationship between hsCRP and infarct.
- ✓ There is no statistically significant relationship between hsCRP and age, sex, smoking and alcohol.

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PROFORMA

NAME: IP NO: SERIAL NO:

AGE:

SEX:

OCCUPATION:

ADDRESS:

DATE AND TIME OF STROKE:

DATE OF ADMISSION :

STROKE: RISK FACTORS

SYSTEMIC HYPERTENSION Y/N

DIABETES MELLITUS Y/N

SMOKING Y/N

ALCOHOLISM Y/N

HIGH CHOLESTEROL Y/N

IHD Y/N

RHD Y/N

AF Y/N

PAST HISTORY OF STROKE : Y/N

CLINICAL EXAMINATION:

PULSE RATE: BP:

CVS:

RS:

ABDOMEN:

CNS:

ACUTE STROKE SYMPTOMS AND SIGNS

SYMPTOMS

HEADACHE

GIDDINESS

LOSS OF CONSCIOUSNES

VOMITING

GAIT DISTURBANCE

CONVULSIONS

SPEECH DEFICIT

SIGNS

SPEECH DEFICIT

HEMIANOPIA

DIPLOPIA

MOTOR SYSTEM

PARESIS AT ANY SITE

PARESIS OF ARMS Y/N R/L/B

PARESI OF LEGS Y/N R/L/B

PARESIS OF FACE Y/N R/L/B

FIRST INVOLVED FACE / ARMS / LEGS

NO SUCH ORDER Y/N

SENSORY DEFICIT Y/N

CEREBELLAR SIGNS Y/N

NIHSS SCORE AT THE TIME OF ADMISSION – MILD / MODERATE / SEVERE

MRS AFTER 4 WEEKS : 00/01/02/03/04/05/06

INVESTIGATIONS:

HB%:

TOTAL COUNT:

DIFFERENTIAL COUNT P- , L- , E- , M- , B-

ESR:

HS-CRP:

BLOOD UREA:

BLOOD SUGAR:

SERUM CREATININE:

SERUM ELECTROLYTES:

SERUM CHOLESTEROL:

ECG:

CT BRAIN AND FINDING :

HAEMORRHAGE : Y/N

INFARCT : Y/N

LOCATION : ACA/MCA/PCA

WATER SHED/GLOBAL/LACUNAR/OTHERS

NAME	AGE	SEX	RISK FACTORS					CLINICAL FEATURES					TERRITORY OF INFARCT				hsCRP	NIHSS			MRS	
			SMOKING	ALCOHOL	DIABETES	HTN	CHOLOSTEROL	LOC	CN(F/V)	SP.DIS	RT.WEAKNESS	LT.WKNESS	ACA	MCA	PCA	LAC/GLO/W		MILD	MODER	SEVERE	POOR	GOOD
AMASI	68	M	Y	Y	N	Y	Y	N	F	Y	Y	N	-	Y	-	-	3.8	-	14	-	4	-
KANDAN	57	M	N	Y	N	Y	N	N	F	Y	Y	N	-	Y	-	-	2.9	-	10	-	3	-
PERUMAL	70	M	Y	Y	Y	N	Y	Y	F	Y	Y	N	-	Y	-	-	6.8	-	-	23	6	-
KANIYAN	56	M	Y	Y	N	N	N	N	F	N	N	Y	-	-	-	L	2	-	7	-	-	1
JOTHI	68	F	N	N	Y	Y	Y	Y	V	Y	N	Y	-	Y	-	-	5	-	-	22	5	-
CHANDRA	61	F	N	N	Y	Y	Y	N	F	Y	Y	N	Y	-	-	-	3.4	-	-	20	4	-
HARIHARAN	41	M	Y	Y	N	Y	Y	Y	F	Y	N	Y	-	Y	-	-	4.2	-	-	25	5	-
GURU	57	M	N	Y	Y	N	Y	N	V	Y	Y	N	-	-	-	L	2.9	-	13	-	3	-
MANI	72	M	Y	Y	N	Y	N	N	F	Y	Y	N	Y	-	-	-	2.5	-	4	-	-	2
NAGARAJ	69	M	Y	Y	Y	Y	Y	N	F	Y	N	Y	Y	-	-	-	2	-	9	-	-	1
NALINI	68	F	N	N	Y	N	N	N	N	Y	N	Y	-	-	-	L	2.8	-	7	-	-	1
CHANDRAN	76	M	N	Y	Y	Y	Y	Y	V	Y	Y	N	-	-	-	L	6.9	-	-	26	6	-
DEVARAJ	79	M	Y	N	N	N	N	N	F	Y	N	Y	-	Y	-	-	2.9	-	8	-	-	2
DURAI	60	M	Y	Y	Y	N	Y	Y	F	Y	N	Y	-	-	Y	-	2.8	-	14	-	3	-
GUNALAN	58	M	Y	N	N	N	N	N	N	N	N	Y	Y	-	-	-	2.3	-	8	-	-	1
AMMANI	78	F	N	N	Y	N	Y	N	F	N	N	Y	-	Y	-	-	3.8	-	14	-	3	-
GOWRI	50	F	N	N	Y	N	Y	Y	F	Y	Y	N	-	Y	-	-	4.4	-	-	18	4	-
ASHOK	36	M	N	Y	Y	Y	Y	N	F	N	N	Y	-	Y	-	-	5.1	-	-	15	3	-
ALAGU	60	M	Y	Y	Y	N	N	N	F	Y	Y	N	-	Y	-	W	3.2	-	7	-	-	2
BALAGURU	45	M	N	Y	Y	N	Y	N	N	N	N	Y	-	-	-	-	2.1	-	9	-	-	2
CHINNAIYA	68	M	Y	N	N	N	Y	N	F	Y	Y	N	Y	-	-	-	2.7	-	10	-	3	-
HARINI	56	F	N	N	Y	N	Y	N	F	Y	Y	N	-	Y	-	-	5.5	-	-	16	5	-
KANI	72	F	N	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	4.2	-	-	18	5	-
PETHI	56	F	N	N	Y	Y	Y	Y	F	Y	Y	N	-	Y	-	-	6.4	-	-	27	6	-
AKILAN	43	M	Y	N	N	N	N	N	N	N	N	Y	-	-	-	L	2.5	-	6	-	-	2
KAMAL	28	M	N	N	Y	N	Y	N	F	Y	Y	N	-	Y	-	-	3.7	-	-	18	4	-
MOORTHY	56	M	Y	Y	Y	N	Y	Y	F	Y	Y	N	-	Y	-	-	6.4	-	-	24	6	-
AKILA	69	F	N	N	Y	N	Y	N	F	Y	N	Y	Y	-	-	L	3.2	-	8	-	-	2
SARASU	70	F	N	N	Y	N	Y	N	F	N	N	Y	-	-	-	-	2.5	-	13	-	3	-
INDIRAN	46	M	Y	Y	Y	Y	Y	Y	F	Y	Y	N	-	Y	-	-	4.8	-	-	19	5	-
LALITHA	56	F	N	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	3.5	-	-	12	-	2
MANI	63	M	Y	Y	Y	Y	Y	Y	F		Y	N	-	Y	-	-	5.8	-	-	24	6	-
MARIAMMAL	67	F	N	N	N	N	N	N	F	N	N	Y	Y	-	-	-	1.2	-	6	-	-	1
LOGESH	45	M	Y	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	2.8	-	13	-	3	-
NALLAMMAL	71	F	N	N	Y	Y	Y	Y	F	Y	Y	N	-	Y	-	-	3.4	-	-	16	3	-
MALARVIZHI	35	F	N	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	2.5	-	10	-	-	2
MARISWA	54	F	N	N	N	N	N	N	N	Y	N	Y	-	-	-	L	2	-	7	-	-	1

RI																						
OCHAPPAN	72	M	N	Y	Y	N	N	N	F	N	Y	N	Y	-	-	-	2.1	-	7	-	-	1
PARVATHI	68	F	N	N	Y	Y	Y	N	N	N	Y	N	-	Y	-	-	3.5	-	14	-	3	-
NAGESWARI	50	F	N	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	2.8	-	12	-	-	2
MUTHU	69	M	Y	Y	Y	Y	Y	Y	F	Y	N	Y	-	-	-	G	5.1	-	-	25	6	-
RAKKU	70	F	N	N	Y	N	Y	N	F	Y	N	Y	-	Y	-	-	3.4	-	14	-	3	-
RAMYA	50	F	N	N	Y	N	Y	N	N	N	N	Y	-	-	Y	-	2.6	-	7	-	-	2
DEVADAS	78	M	Y	Y	Y	Y	Y	Y	F	Y	Y	N	-	Y	-	-	4	-	-	16	4	-
FAZIL	68	M	Y	Y	Y	Y	Y	N	F	Y	N	Y	-	Y	-	-	3.7	-	-	15	4	-
ISMAIL	58	M	Y	N	Y	N	Y	N	F	Y	Y	N	-	Y	-	-	3.9	-	14	-	3	-
AIYSHA	69	F	N	N	Y	N	Y	N	F	N	N	Y	Y	-	-	-	3.1	-	5	-	-	2
SAMSATH	56	F	N	N	Y	Y	Y	N	F	Y	Y	N	Y	-	-	-	2	-	5	-	-	1
ELAVANIL	70	M	Y	N	Y	N	N	N	F	Y	N	Y	-	Y	-	-	2	-	7		-	2
GANESH	70	M	Y	Y	Y	Y	Y	Y	F	Y	N	Y	-	Y	-	-	4.1	-	-	16	5	-

Key words

M- Male

F- Female

Y-Yes

N- No

LOC- Loss Of Conscious

F-Facial Palsy (Column 10)

V-Visual Disturbances

Sp.Dis- Speech Disturbances

L/G/W- Lacunar / Globular / Watershed infarct

ABBREVIATIONS

1. ACA- Anterior Cerebral Artery
2. AF- Atrial Fibrillation
3. aPTT- Activated Partial Thromboplastin Time
4. C3 AND C4- Complements C3 And C4
5. CT- Computed Tomography
6. CRP- C-Reactive Protein
7. CVA-Cerebrovascular Accidents
8. hsCRP- Highly Sensitive C-Reactive Protein
9. HB- Haemoglobin
10. IHD-Ischemic Heart Disease
11. MCA-Middle Cerebral Artery
12. MRI- Magnetic Resonance Imaging
13. MRS-Modified Rankin Scale
14. NIHSS-National Institute Of Health Stroke Scale
15. PCA- Posterior Cerebral Artery
16. RHD- Rheumatic Heart Disease
17. rt-PA- Recombinant Tissue Plasminogen Activator
18. UMN- Upper Motor Neuron

Depart of Medi

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Madurai.20. Dated: .08.2012

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Sub: Establishment-Govt. Rajaji Hospital, aMadurai-20-
Ethics committee-Meeting Agenda-communicated-regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held at 11.00 Am to 1.00Pm on 28.06.2012 at the Dean Chamber, Govt. Rajaji Hospital, Madurai. The following members of the committee have been attended the meeting.

---

1. Dr.N.Vijayasankaran,M.ch(Uro.) 094-430-58793 0452-2584397	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
2. Dr.P.K. Muthu Kumarasamy, M.D., 9843050911	Professor & H.O.D of Medical, Oncology(Retired)	Member Secretary
3. Dr.T.Meena,MD 094-437-74875	Professor of Physiology, Madurai Medical College	Member
4. Dr. S. Thamilarasi, M.D (Pharmacol)	Professor of pharmacology	
5.Dr.Moses K.Daniel MD(Gen.Medicine) 098-421-56066	Professor of Medicine Madurai Medical College	Member
6.Dr.M.Gobinath,MS(Gen.Surgery)	Professor of Surgery Madurai Medical College	Member
7.Dr.S. Dilshadh, MD(O&G) 9894053516	Professor of OP&Gyn Madurai Medical College	Member
8.Dr.S.Vadivel Murugan., M.D, 097-871-50040	Professor of Medicine Madurai Medical College	Member

Sl. No	Name of P.G.	Course	Name of the Project	Remarks
1.	Dr. Rajkumar. J	M.D Gen med	High-Sensitivity CRP assay as a prognostic indicator in cerebrovascular accidents.	Approved

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8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

17.8.12

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To

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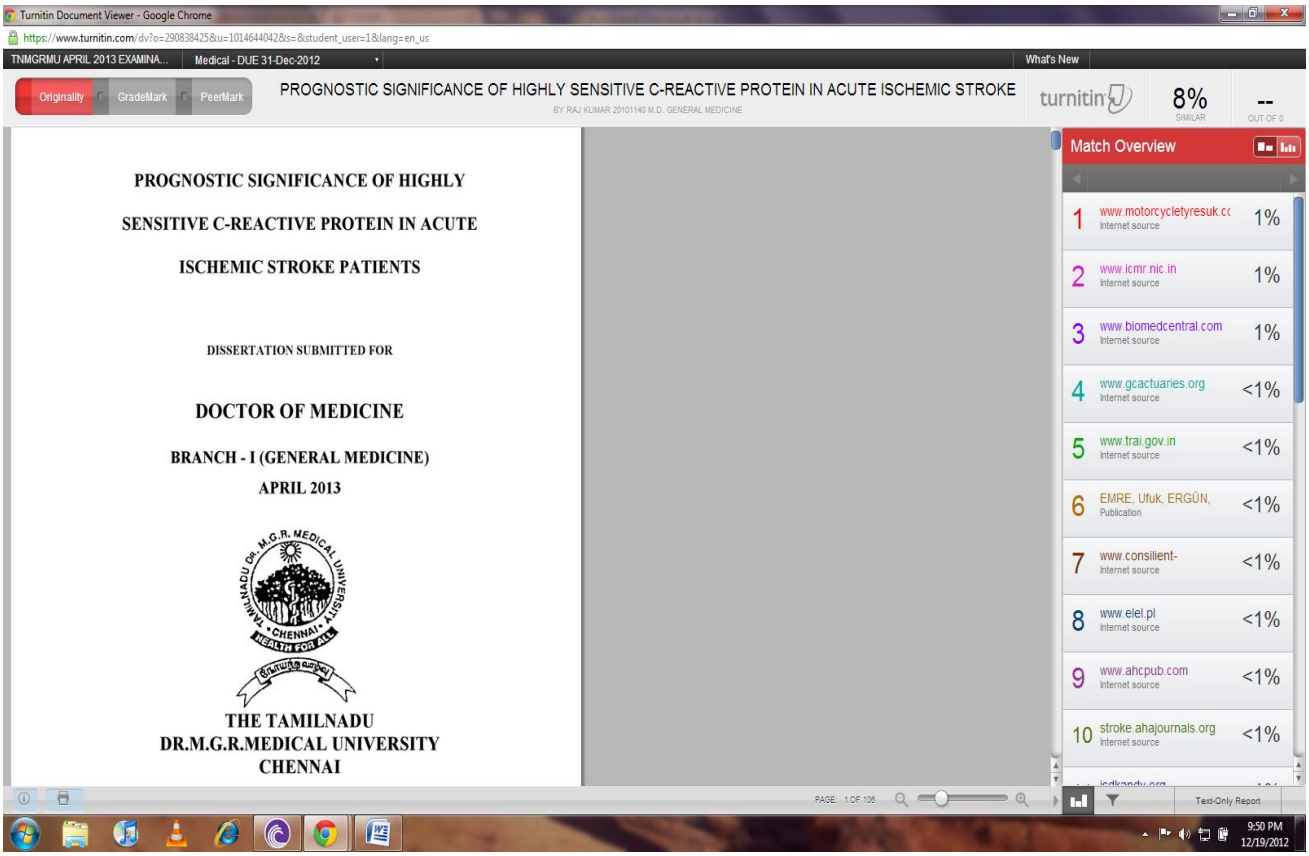
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E-mail	dr.xavierraj@gmail.com
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PROGNOSTIC SIGNIFICANCE OF HIGHLY SENSITIVE C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE PATIENTS DISSERTATION SUBMITTED FOR DOCTOR OF MEDICINE BRANCH - I (GENERAL MEDICINE) APRIL 2013 THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY CHENNAI BONAFIDE CERTIFICATE This is to certify that the dissertation entitled “PROGNOSTIC SIGNIFICANCE OF HIGHLY SENSITVE C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE PATIENTS” submitted by Dr.J.RAJ KUMAR to the Tamil Nadu Dr. M.G.R.Medical University, Chennai in partial fulfillment of the requirement for the award of M.D Degree Branch I (General Medicine) is a bonafide research work was carried out by him under my direct supervision & guidance. Prof.Dr.M.NATARAJAN...

Depart of Medi

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Govt. Rajaji Hospital,
Madurai.20. Dated: .08.2012

Institutional Review Board / Independent Ethics Committee.
Dr. N. Mohan, M.S., F.I.C.S., F.A.I.S.,
Dean, Madurai Medical College & 2521021 (Secy)
Govt Rajaji Hospital, Madurai 625020.
Convenor
grhethicssecy @gmail.com.

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9.Shri.M.Sridher,B.sc.B.L. 099-949-07400	Advocate, 2, Deputy collectors colony 4th street KK Nagar, Madurai-20.	Member
10.Shri.O.B.D.Bharat,B.sc., 094-437-14162	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
11.Shri. S.sivakumar,M.A(Social) Mphil 093-444-84990	Sociologist, Plot No.51 F.F, K.K Nagar, Madurai.	Member

Following Projects were approved by the committee

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To
All the above members and Head of the Departments concerned.
All the Applicants.